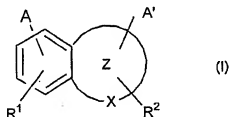


CLAIMS:

1. A method for selective targeting of a chemical compound to a cell undergoing perturbation of the normal organization of its plasma membrane (PNOM-cell) present in a cell population, comprising the steps of: (i) contacting the cell population with a PMBC, being a chemical compound represented by the structure set forth in formula (I):



wherein Z represents null, or a ring system formed of cycloalkyl, cycloalkenyl, heterocyclyl, aryl or heteroaryl groups or combinations of such groups, the ring system consisting of 5, 6, 7, 8, 9 or 10 atoms;

X represents an atom, which is C, N, O or S, where each of these atoms may bear 0, 1 or 2 hydrogen atoms according to the meaning of Z;

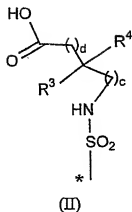
R¹ and R² are each independently hydrogen, halogen, hydroxyl, -NO₂ group or W-Q_b; wherein W is null, nitrogen, oxygen or carbon; and Q represents hydrogen, a C₁, C₂, C₃, C₄, C₅ or C₆ alkyl, hydroxyalkyl, or straight or branched haloalkyl, wherein Q groups may be either the same or different; and

b is an integer, being 1 when W is oxygen or null; 2 in the case that W is nitrogen; or 3 in the case that W is a carbon atom;

A and A' are each a radical independently selected from one of the following four groups:

- i) hydrogen;
- ii) SO₃H, and L-SO₃H, wherein L stands for a C₁, C₂, C₃, C₄ or C₅ alkylene linker;
- iii) a structure, set forth in formula II:

57



wherein

5 R^3 is hydrogen, $(CH_2)_p-OH$, $(CH_2)_p-SH$, $(CH_2)_p-F$, or suspected of comprising such PNOM cell, comprising the steps of contacting a cell population with a compound represented a radical of C_1 , C_2 , C_3 , or C_4 carboxylic acid, wherein p is 1, 2, or 3;

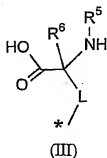
10 R^4 is hydrogen, a C_1 , C_2 , C_3 , C_4 , C_5 C_6 straight or branched alkyl, a C_1 , C_2 , C_3 , C_4 , C_5 C_6 straight or branched hydroxyalkyl or a C_1 , C_2 , C_3 , C_4 , C_5 C_6 straight or branched fluoroalkyl;

c and d are each an integer of 0 or 1; c and d may be the same or different;

* represents the point of attachment to the structure of formula (I); or

iv) a structure set forth in formula (III):

15



20 wherein R^5 and R^6 are independently hydrogen, C_1 , C_2 , C_3 , C_4 , C_5 , C_6 straight or branched alkyl, C_1 , C_2 , C_3 , C_4 , C_5 , C_6 straight or branched hydroxyalkyl or C_1 , C_2 , C_3 , C_4 , C_5 , C_6 straight or branched haloalkyl; R^5 and R^6 can be the same or different; and L stands for null or a C_1 , C_2 , C_3 , C_4

or C₃ alkylene linker; * represents the point of attachment to the structure of formula (I);

wherein when the at least one of A or A' groups is other than hydrogen, then the at least other of A or A' groups is different than the structure of formula (III);

thereby selectively targeting the chemical compound to the PNOM-cells within the cell population.

2. A method of detecting the presence of PNOM-cells within a cell population, comprising the steps of:

(i) contacting the cell population with a PMBC, or a conjugate comprising said PMBC and a marker for imaging, wherein said PMBC is represented by the structure set forth in formula (I) of claim 1, wherein A, A', X, Z, R¹, R², R³, R⁴, R⁵, R⁶, L, c and d are as defined in Claim 1; and

(ii) determining the amount of PMBC bound to said cells, wherein a bound amount which is significantly higher than control indicates the presence of PNOM-cells within the cell population.

3. A method for detecting the presence of PNOM-cells in a tissue in a patient or an animal, comprising the steps of:

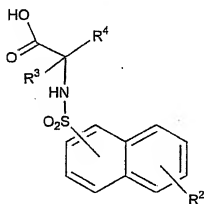
(i) administering a PMBC, or a conjugate comprising said PMBC and a marker for imaging to a human or an animal, wherein said PMBC is represented by the structure set forth in formula (I) according to claim 1, wherein A, A', X, Z, R¹, R², R³, R⁴, R⁵, R⁶, L, c and d are as defined in Claim 1; and

(ii) determining the amount of PMBC bound to cells in said tissue, wherein an amount of compound bound to cells in a tissue which is significantly higher than the control indicates its being a PNOM-cell containing tissue.

4. The method according to any one of Claims 1-3, wherein the PNOM-cell is a cell undergoing a death process, an apoptotic cell or an activated platelet.

5. The method according to any one of Claims 1-3, wherein the PNOM-cell is in the body, organ, tissue, tissue culture or body fluid.

6. A method according to any one of Claims 1-5, wherein in the compound represented by the structure as set forth in formula (I), wherein A or A' are represented by formula (II), R¹ is hydrogen, and R² is NQ₂, wherein Q groups may be the same or different, each being a hydrogen or a C₁-C₄ alkyl.
- 5 7. A method according to any one of Claims 1-5, wherein said PMBC is represented by the structure as set forth in formula (IV):

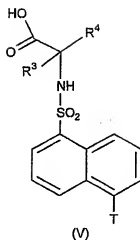


(IV)

wherein R², R³ and R⁴ are as defined in Claim 1.

- 10 8. A method according to Claim 3, for the detection of cell death in a disease characterized by occurrence of apoptosis.
9. A method according to Claim 3, for the detection of activated platelets in a disease characterized by blood clotting.
10. A method according to Claim 3, for detection of apoptotic cells within a
- 15 tumor.
11. A method according to Claim 3, for monitoring the response of a tumor to anti-cancer treatment.
12. A method according to Claim 3, for monitoring of apoptosis in normal tissues during anticancer treatment, said apoptosis of normal tissue being an
- 20 adverse effect of said treatment.
13. A compound represented by a structure as set forth in formula (V):

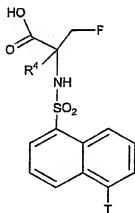
60



wherein T is $-\text{OH}$, $-\text{O}-\text{CH}_3$, $-\text{O}-(\text{CH}_2)_y\text{CH}_3$, NH_2 , $\text{N}(\text{CH}_3)_2$, $-\text{N}[(\text{CH}_2)_3\text{CH}_3]_2$, $-\text{N}(\text{CH}_3)[(\text{CH}_2)_2\text{CH}_3]$, $-\text{N}(\text{CH}_3)\text{CH}_2\text{CH}_3$ or $-\text{N}(\text{CH}_3)[(\text{CH}_2)_3\text{CH}_3]$; y stands for an integer of 1, 2, or 3; and R^3 and R^4 are each

5

14. A compound according to Claim 13, represented by the structure as set forth in formula (VI):

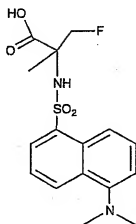


(VI)

wherein T is as defined in Claim 13, and R^4 is hydrogen or a C_1 , C_2 , C_3 , C_4 , C_5 or C_6 straight or branched alkyl, and wherein the F atom is ^{18}F or ^{19}F or mixtures of fluorine isotopes.

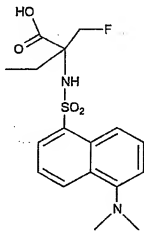
10

15. A compound according to Claim 13, represented by the structure as set forth in formula (VII):



wherein the F atom is ¹⁸F or ¹⁹F or mixture of fluorine isotopes.

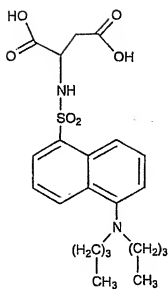
16. A compound according to Claim 13, represented by the structure as set forth in formula (VIII):



wherein the F atom is ¹⁸F or ¹⁹F or mixtures of fluorine isotopes.

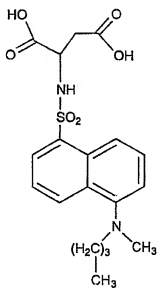
17. A compound according to Claim 13 represented by the structure as set forth in formula (IX):

62



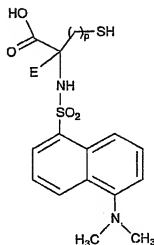
(IX)

18. A compound according to Claim 13, represented by the structure as set forth in formula (X):



(X)

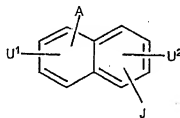
19. A compound according to Claim 13, represented by the structure as set forth in formula (XI):



(XI)

wherein E is C_1 , C_2 , C_3 or C_4 alkyl; C_1 , C_2 , C_3 or C_4 fluoroalkyl; or C_1 , C_2 , C_3 or C_4 hydroxyalkyl; p stands for an integer of 1 or 2.

20. A compound according to Claim 13, wherein p is 1.
21. A method of selective targeting a PNOM-cell in a cell population comprising the steps of contacting a cell population with a compound represented by the structure as set forth in formula (XII):



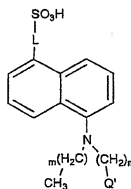
(XII)

- wherein A is SO_3H or $L-SO_3H$, wherein L stands for a substituted or unsubstituted C_1 , C_2 , C_3 , C_4 or C_5 alkylene;
- J is selected from SO_3H , $L-SO_3H$, wherein L is as defined above, hydrogen and $W-Q$; wherein W is null, nitrogen, oxygen or carbon; and Q represents hydrogen, a C_1 , C_2 , C_3 , C_4 , C_5 or C_6 straight or branched alkyl, straight or branched hydroxyalkyl, or straight or branched

haloalkyl; wherein Q groups may be either the same or different; b is an integer, being 1 when W is oxygen or null, 2 in the case that W is nitrogen, or 3 in the case that W is a carbon atom;

U¹ and U² are each halogen, halogen, hydroxyl, -NO₂; C₁, C₂, C₃, C₄, C₅ or C₆ straight or branched alkyl; C₁, C₂, C₃, C₄, C₅ or C₆ straight or branched halo-alkyl; C₁, C₂, C₃, C₄, C₅ or C₆ straight or branched hydroxy-alkyl; U¹ and U² groups may be the same or different.

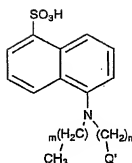
22. A method of selective targeting a PNOM-cell in a cell population, comprising the steps of contacting a cell population with a compound represented by the structure as set forth in formula (XIII):



(XIII)

wherein n stands for an integer of 1, 2, 3, 4, 5 or 6, m stands for an integer of 0, 1, 2 or 3, Q' is hydrogen, -OH or -F, and L stands for null or C₁, C₂, C₃, C₄ or C₅ alkylene, thereby selectively targeting a PNOM-cell in said cell population.

23. A method of selective targeting a PNOM cell in a cell population suspected of comprising such a PNOM-cell, comprising the steps of contacting a cell population with a compound represented by the structure as set forth in formula (XIV);

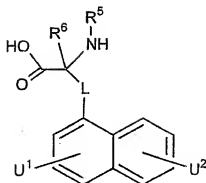


(XIV)

wherein n stands for an integer of 1, 2, 3, 4, 5 or 6, m stands for an integer of 0, 1, 2 or 3 and Q' is hydrogen, -OH or -F.

- 5 24. A compound represented by the structure set forth in formula (XIV)
wherein Q' is F being either ¹⁸F or ¹⁹F or a mixture of isotopes.
25. A compound represented by the structure set forth in formula (XIV)
wherein m is 0, n is 4 and Q' is hydrogen.
26. A compound represented by the structure set forth in formula (XIV)
10 wherein m is 0, n is 3 and Q' is hydroxyl.
27. A compound represented by the structure set forth in formula (XIV)
wherein m is 0, n is 4 and Q' is fluorine.
28. A method of selective targeting PNOM-cells in a cell population
suspected of comprising such PNOM-cells, comprising the steps of contacting a
15 cell population with a compound represented by the structure as set forth in
formula (XV):

66



(XV)

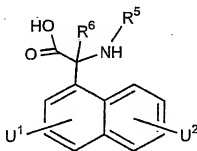
wherein R^5 and R^6 are each independently hydrogen, C_1 , C_2 , C_3 , C_4 , C_5 , C_6 straight or branched alkyl, straight or branched hydroxyalkyl or straight or branched fluoroalkyl; R^5 and R^6 can be the same or different;

L stands for null or a C_1 , C_2 , C_3 , C_4 or C_5 alkylene linker;

U^1 and U^2 are each hydrogen, halogen, hydroxyl, $-NO_2$; C_1 , C_2 , C_3 , C_4 , C_5 or C_6 straight or branched alkyl; C_1 , C_2 , C_3 , C_4 , C_5 or C_6 straight or branched haloalkyl; C_1 , C_2 , C_3 , C_4 , C_5 or C_6 straight or branched hydroxyalkyl; U groups may be the same or different.

29. A compound represented by the structure as set forth in formula (XV), wherein either U^1 or U^2 is fluorine or C_1 , C_2 , C_3 or C_4 fluoroalkyl, the F atom being either ^{18}F or ^{19}F .

30. A method of selective targeting PNOM-cells, comprising the steps of contacting a cell population with a compound represented by the structure as set forth in formula (XVI):



(XVI)

wherein R⁵ and R⁶ are independently hydrogen, C₁, C₂, C₃, C₄, C₅, C₆ straight or branched alkyl, straight or branched hydroxyalkyl or straight or branched fluoroalkyl; R⁵ and R⁶ can be the same or different; U¹ and U² are each
5 hydrogen, halogen, hydroxyl, -NO₂; C₁, C₂, C₃, C₄, C₅ or C₆ straight or branched alkyl; C₁, C₂, C₃, C₄, C₅ or C₆ straight or branched haloalkyl; C₁, C₂, C₃, C₄, C₅ or C₆ straight or branched hydroxyalkyl; U groups may be the same or different.

31. A compound represented by the structure as set forth in formula (XVI),
10 wherein R⁵ is C₁, C₂, C₃, C₄, C₅, C₆ straight or branched alkyl, straight or branched hydroxyalkyl and straight or branched fluoroalkyl; R⁶ is C₂, C₃, C₄, C₅, C₆ straight or branched alkyl, straight or branched hydroxyalkyl or straight or branched fluoroalkyl; and either U¹ or U² is other than hydrogen.

32. A method of detecting PNOM cells in a population of cells, comprising
15 the steps of:

(i) contacting the cell population with a PMBC, or a conjugate comprising said PMBC and a marker for imaging, wherein said PMBC is represented by the structure set forth represented in any one of formulae I, IV, V, VI, VII, VIII, IX, X, XI, XII, XIII, XIV, XV or XVI; and
20 (II) determining the amount of PMBC bound to cells in said cell population,
wherein a bound amount which is significantly higher than control indicates the presence of PNOM-cells within the cell population.

33. A method for detecting the presence of PNOM-cells in a tissue in a patient
25 or an animal, comprising the steps of:

(i) administering a PMBC, or a conjugate comprising said PMBC and a marker for imaging to a human or an animal, wherein said PMBC is represented by the structure set forth in any one of formulae I, IV, V, VI, VII, VIII, IX, X, XI, XII, XIII, XIV, XV or XVI; and
30 (ii) determining the amount of PMBC bound to cells in said tissue, wherein an amount of compound bound to cells in a tissue which is

significantly higher than the control indicates its being a PNOM-cell containing tissue.

34. A compound according to any one of claims 13-20, 24-27, 29, and 31, wherein said compound is being linked either directly or through a linker Y to a member
5 selected from a solid support, a marker for imaging or a therapeutic drug, wherein said linker Y is C₁, C₂, C₃, C₄, C₅ or C₆ alkylene, 5-6 atom aromatic or 5-6 heteroaromatic ring, wherein the heteroatom of said heteroaromatic ring is N, O and S, a metal chelator, or combinations thereof.
35. An agent for the detection of PNOM-cells, comprising a compound according
10 to any one of the claims 13-20, 24-27, 29, and 31, wherein said compound is linked or comprises a marker for imaging.
36. An agent according to claim 35 wherein said marker for imaging is detectable by detector of color, fluorescence, X-ray, CT scan, MRI, radio-isotope scan, SPECT, or PET scan.
37. A method for labeling a compound according to claims 13-20 with a marker
15 for PET imaging, said method comprising:
- (i) attaching a marker for PET imaging to an amine subunit of said compound;
 - (ii) linking said amine subunit with a sulfonic acid subunit via formation of a
20 sulfonamide bond.
38. The method according to claim 37, further comprising the step of protecting the functional groups of said amine subunit and/or said sulfonic acid subunit by appropriate protecting groups.
39. The method according to claim 37, further comprising a step of purification.
- 25 40. The method according to claim 37, further comprising the step of removing of said protecting groups after the step of attaching the marker for PET imaging and/or after the step of linking said amine subunit with the sulfonic acid subunit.
41. The method for labeling a compound of claim 37, wherein said marker for PET imaging is ¹⁸F.